

DECLARATION

I, the undersigned Michael David, MD, a citizen of Israel residing in Tel Aviv, Israel hereby declare as follows:

1) I hold a M. D. degree from Hadassah Medical School, Hebrew University, Jerusalem, Israel. I am currently employed as a doctor at Rabin Medical Center, Petah Tiqva, Israel. I have been and I am currently involved in research related *inter alia* to the field of dermatology.

My CV is attached to this declaration as Annex A.

2) I have been requested by the Applicant to review the literature regarding the location of tattoo pigments in support of arguments being presented in the process of prosecution of US patent application number 10/560,063. The results of my review are:

a) Most tattoo pigment particles are localized to lysosomes within mononuclear cells in the dermis, i.e fibroblasts, macrophages, and occasional mast cells (Lipper & Rox Anderson, in: Fitzpatrick's Dermatology in General Medicine, sixth edition, 2003).

b) Ferguson et al. examined biopsies obtained from 35 amateur and professional tattoos including black and coloured tattoos (Br J Dermatol, 1997) and found pigment-laden cells which were clustered around small vessels on the papillary dermis and around vessels, hair follicles and sebaceous glands in the reticular dermis. In general, tattoo pigment was more abundant in the reticular dermis than in the papillary dermis. Occasional cells containing pigment were found in the subcutaneous fat and around eccrine glands. The depth of pigment varied within and between different tattoos. The mean depth measured from the granular layer was 2mm and ranged from 1.1 to 2.9mm. The dermal collagen appearance was not altered by the tattoo. At the ultrastructural level, tattoo pigment was exclusively intracellular: individual pigment particles and clumps of particles were sequestered within membrane-bound spherical structures,

identified as secondary lysosomes in fibroblasts, macrophages as well as in mast cells.

c) In an earlier ultrastructural study on human tattoo, conducted by Lea and Pawlowski, ink particles were found to be located exclusively within dermal fibroblasts(Int J Dermatol, 1987).

d) Similar conclusion confirming the presence of most of tattoo particles in the dermal fibroblasts and macrophages was demonstrated in a recent study conducted by us on pig skin.

3) I have also been asked by the Applicant to give an opinion regarding the timing of the phagocytosis, i.e. the process by which the particles are swallowed by the cells. I didn't find any reference to this subject in the literature. In my opinion the process takes place in a matter of days after the tattoo is created.

4) I hereby declare that all statements made herein of my own knowledge are true and that all statements made herein on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the subject application or any patent issuing thereon.

5) The name and signature below are my name and signature.

This __ day of June, 2007

Michael David, MD